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Neurosyphilis presenting as a new onset lateralized movement disorder

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Abstract: We report a unique and illustrative case of a 52-year-old man with neurosyphilis presenting as subacute hemichorea, and discuss a vascular, metabolic or inflammatory origin. A broad range of neurological findings may be linked to neurosyphilis, potentially complicating its diagnosis. We propose that new onset lateralized movement disorders may constitute the initial clinical presentations of neurosyphilis, and provide evidence for striatal hypermetabolism pointing to direct inflammatory, syphilitic changes as the underlying pathophysiological mechanism. Neurosyphilis is no longer a common disorder, but the prevalence of syphilis is rising again in Western countries and its past reputation as the great imitator should not be forgotten.

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1 **Neurosyphilis presenting as a new-onset lateralized movement disorder**

2 Running title: Neurosyphilis presenting with hemichorea

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Abstract

A broad range of neurological findings may be linked to neurosyphilis, potentially complicating its diagnosis. Here we report a unique and illustrative case of neurosyphilis presenting as subacute hemichorea in a 52-year-old patient and discuss a vascular, metabolic or inflammatory origin. We propose that new-onset lateralized movement disorders may constitute the initial clinical presentation in neurosyphilis and provide evidence for striatal hypermetabolism, pointing to direct inflammatory, syphilitic changes as underlying pathophysiological mechanism. Neurosyphilis is no longer a common disorder, but the prevalence of syphilis is rising again in Western countries and its past reputation as the great imitator should not be forgotten.

Case report

A 52-year old male presented to our clinic with a 3-week history of involuntary irregular movements of the right arm, leg and face, emotional instability and concentration problems. On clinical examination a fluctuating right-sided hemichorea was noted (see online video 1), otherwise the neurological and general exam was normal. The medical history revealed type 2 diabetes and arterial hypertension. There was no personal or family history for neurological disorders.

Cranial magnetic resonance imaging (MRI) demonstrated no focal lesions on FLAIR (fluid attenuated inversion recovery, figure 1a) and diffusion weighted imaging (DWI), while MR angiography showed a focal (<50%) stenosis of the M1 segment of the left middle cerebral artery (MCA). By serum and cerebrospinal fluid (CSF) analysis the diagnosis of neurosyphilis (tertiary meningovascular syphilis) was made based on CSF lymphocytic pleocytosis (396 cells/ μ l; normal range: <5 cells/ μ l), an increased CSF protein (1019 mg/l; normal range: <500mg/l), an TPPA-CSF/serum index of 332.5 (Treponema pallidum particle agglutination index; normal range: <70) and a CSF-VDRL titer of 1:4 (venereal disease research laboratory test; normal range: negative). No evidence for earlier signs of primary (chancres) or secondary (rash) syphilis could be taken from the patient's history. Additional routine laboratory blood tests including screening for human immunodeficiency virus (HIV) were negative apart from elevated spontaneous serum glucose levels up to 14.9mmol/l (normal range: < 11.1mmol/l). Neuropsychological examination revealed substantially impaired motor learning, other parameters tested were in the age- and education-matched normal range.

In line with the clinical presentation, brain fluorodeoxyglucose positron emission tomography (FDG-PET) in the acute stage revealed a markedly asymmetric radiotracer uptake with higher uptake in the left striatum compared to the right striatum, pointing to direct inflammatory, syphilitic changes (figure 1b) as cause of the right-sided hemichorea. No perivascular hypermetabolism in the territory of the left MCA could be seen on FDG-PET.

After a 14-day treatment course with high-dose intravenous penicillin symptoms disappeared completely and CSF pleocytosis substantially improved at follow-up spinal taps three (19 cells/ul) and nine months (22 cells/ul) later. On follow-up brain FDG-PET eight months after initiation of treatment the asymmetry of striatal radiotracer uptake had disappeared (figure 1c).

Discussion

This is the first case reported with new-onset hemichorea as presenting symptom in neurosyphilis. So far only three cases with choreatic movement disorders (reviewed by Shah and Lang [1]) in patients with syphilis are described: one patient developed hemiparesis and subsequently hemichorea on the same side [2]; one patient with neurosyphilis and HIV co-infection showed generalized chorea [3], and one patient suffered over ten years from a generalized chorea due to neurosyphilis [4]. In two reports from the pre-penicillin era Huntington's disease could not be excluded as cause of the symptoms [1].

The pathogenetic mechanism causing hemichorea could not be fully determined in the presented case. Cross-reactive antibodies recognizing neuronal surface structures analog to Sydenham chorea or primary anti-phospholipid antibody syndrome could be one explanation, however we could not detect antibodies against NMDA-R, AMPA-R, GABA(B)-R, mGluR1, mGluR5, LG1 or Caspr2. Cross reactive antibodies to phospholipids like cardiolipin are found in different conditions causing hemichorea (Sydenham chorea, lupus, primary anti-phospholipid antibody syndrome) and may be of pathogenetic relevance. Parenchymal spread of bacteria causing cellular inflammation would be another possible pathomechanism. The rapid clinical improvement of our patient to antibiotic treatment may be an argument for the latter mechanism.

'Neurosyphilis is no longer a common disorder, but the prevalence of syphilis is rising again in Western countries [5] and its past reputation as the great imitator should not be forgotten. Early diagnosis is of great relevance as with penicillin an effective therapy is available.

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Figure / video legend

Figure 1: Neuroimaging

a) Brain MRI in the acute stage showed no structural lesions of the basal ganglia. Depicted is one axial slice of the fluid attenuated inversion recovery (FLAIR) sequence.

b) Brain FDG-PET imaging (axial slice) revealed an asymmetric metabolism with higher uptake in the left striatum compared to the right side at the time of diagnosis.

c) FDG-PET (axial slice) eight months later showed symmetric FDG uptake of both striata. At this time point hemichorea could not be observed anymore.

Supplementary online video 1

Contributed by the patient for publication.

Depicted is the above mentioned patient a few days before admission to our hospital. While he is trying to work at the computer, choreatic movements of the right arm, leg and face are occurring.

Abbreviations not spelled out in the manuscript for readability:

NMDA-R (N-methyl-D-aspartate receptor)

AMPA-R (α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor)

GABA(B)-R (gamma-aminobutyric acid receptor)

mGluR1 (metabotropic glutamate receptor 1)

mGluR5 (metabotropic glutamate receptor 5)

LG1 (Leucine-rich glioma inactivated-1)

Caspr2 (contactin-associated protein-like 2)

